CCNS Opening Workshop
August 17-21, 2015

SPEAKER TITLES/ABSTRACTS

Peter Bandettini
NIMH

"New fMRI Observations at an Individual Level Using Novel Acquisition, Paradigm, and Processing Approaches"

Our group has been focusing for the past several years on detecting and characterizing ever more subtle and elusive fMRI changes in task-based and resting-state fMRI. Using a strategy involving integration of paradigm design, acquisition, and novel processing approaches, we have had some unique and surprising findings. Specifically, we've been able to a) substantially reduce artifactual time series noise - including motion effects using multi-echo EPI in combination with independent component analysis, b) reveal that nearly the entire brain is active - in unanticipated ways - for even simple tasks, using massive averaging and a model - free approach, c) reveal that "brain reading" can be carried out by simply observing the unique connectivity patterns associated with different ongoing tasks. Furthermore, we show that the locations of the nodes of these "informative" connection changes can differ in location from the typically observed magnitude changes in the brain - thus potentially revealing a previously-undetected class of changes (connectivity rather than just magnitude) with brain activation. In addition, this approach appears to be much more sensitive in detecting ongoing tasks than simple assessment of the magnitude changes. Our primary message in these examples that the integrated implementation of paradigm design, acquisition, and relatively simple processing including can open up novel directions in understanding brain organization at an individual level.

Edward Boyden
MIT

"Tools for Mapping Brain Computations"

Complex biological systems like the brain present a challenge: their molecular building blocks are organized with nanoscale precision, but support physiological processes and computations that occur over macroscopic length scales. To enable the understanding and fixing of such complex systems, we are creating tools that enable molecular-resolution maps of large scale systems, as well as technologies for observing and controlling information processing in such systems. First, we have developed a method for imaging large 3-D specimens with nanoscale precision. We embed a specimen in a swellable polymer, which upon exposure to water expands isotropically in size, enabling conventional diffraction-limited microscopes to do large-volume nanoscopy. Second, we have collaboratively developed strategies to image fast physiological processes in 3-D with millisecond precision, and used them to acquire neural activity maps throughout small organisms. Third, we have collaboratively developed robotic methods to automate single cell analysis in living mammalian brain. Finally, we

have developed a set of genetically-encoded reagents, known as optogenetic tools, that when expressed in specific neurons, enable their electrical activities to be precisely driven or silenced in response to millisecond timescale pulses of light. In this way we aim to enable the systematic mapping, dynamical observation, and control of complex biological systems like the brain.

Uri Eden
Boston University

"Estimating Neural Dynamics using Point Process Models"

Although it is well known that brain areas receive, process and transmit information via sequences of sudden, stereotyped electrical impulses, called action potentials or spikes, most analyses of neural data ignore the localized nature of these events. The theory of point processes offers a unified, principled approach to modeling the firing properties of spiking neural systems, and assessing goodness-of-fit between a neural model and observed spiking data. We develop a point process modeling framework and state space estimation algorithms to describe and track the evolution of dynamic representations from individual neurons and neural ensembles. This allows us to derive a toolbox of estimation algorithms and adaptive filters to address questions of static and dynamic encoding and decoding. These methods will be illustrated through a couple of examples. First, we will model spatially specific spiking activity in the rat hippocampus and use a point process filter to reconstruct the animal's movement trajectory during a spatial navigation task. Next, we will develop a sequential importance sampling procedure for estimating biophysical parameters of conductance based neural models using only the resulting spike times. Issues of model identification and misspecification will also be discussed.

Maxime Descoteaux
Universite de Sherbrooke

"Diffusion MRI Tractography and Connectomics: problems and challenges"

Diffusion magnetic resonance (dMRI) imaging techniques have recently been proposed to overcome the classical limitations of diffusion tensor imaging (DTI). DMRI nowadays opens exciting possibilities in advanced tractography to recover complex fiber crossing configurations but also for microstructure imaging of the white matter. In this talk, we will see how one can go from raw diffusion MRI data to full brain structural connectivity and microstructure estimation of fiber calibers. In particular, we will see how diffusion tractography is currently at the heart of connectomics studies and how it can be combined with microstructure imaging to perform microstructure-informed tracking. Tractography, connectomics and diffusion microstructure imaging are at their infancies and now open a wide range of exciting research questions and computational problems to solve.

Markus Diesmann
Juelich Research Centre

"Brain-Scale Simulations at Cellular and Synaptic Resolution: Necessity and Feasibility"

The cortical microcircuit, the network comprising a square millimeter of brain tissue, has been the subject of intense experimental and theoretical research. The lecture first introduces a full-scale model of this circuit at cellular and synaptic resolution [1]: the model comprises about 100,000 neurons and one billion local synapses connecting them. The purpose of the model is to investigate the effect of network structure on the observed activity. To this end it incorporates cell-type specific connectivity

but identical single neurons dynamics for all cell types. The emerging network activity exhibits a number of the fundamental properties of in vivo activity: asynchronous irregular activity, layer specific spike rates, higher spike rates of inhibitory neurons as compared to excitatory neurons, and a characteristic response to transient input. Despite this success, the explanatory power of such local models is limited as half of the synapses of each excitatory nerve cell have non-local origins and at the level of areas the brain constitutes a recurrent network of networks.

The second part of the lecture therefore argues for the need of brain-scale models to arrive at self-consistent descriptions of the multi-scale architecture of the network. Such models will enable us to relate the microscopic activity to mesoscopic measures [2] and functional imaging data and to interpret those with respect to brain structure. Theoretical arguments support that generally networks cannot be scaled down without perturbation of their correlation structure [3].

The third part of the lecture introduces the technology required to simulate such models and discusses the performance of the present NEST simulation code. Brain-scale networks exhibit a breathtaking heterogeneity in the dynamical properties and parameters of their constituents. Over the past decade researchers have learned to manage the heterogeneity with efficient data structures [4]. Already early parallel codes had distributed target lists, consuming memory for a synapse on just one compute node. As petascale computers with some 100,000 nodes become increasingly available for neuroscience, new challenges arise: Each nerve cell contacts on the order of 10,000 other neurons and thus has targets only on a fraction of all nodes; furthermore, for any given source neuron, at most a single synapse is typically created on any node. The heterogeneity in the synaptic target lists thus collapses along two dimensions: the dimension of the types of synapses and the dimension of the number of synapses of a given type. The latest technology [5] takes advantage of this double collapse using metaprogramming techniques and orchestrates the full memory of petascale computers like JUQUEEN and the K computer into a single brain-scale simulation.

www.nest-initiative.org

[1] Potjans TC, Diesmann M (2014) Cerebral Cortex 24 (3): 785-806
[2] Linden H, Tetzlaff T, Potjans TC, Pettersen KH, Gr\"un S, Diesmann M, Einevoll GT (2011) Neuron 72(5):859-872
[3] van Albada S, Helias M, Diesmann M (2014) arXiv:1411.4770 [q-bio.NC]
[4] Helias M, Kunkel S, Masumoto G, Igarashi J, Eppler JM, Ishii S, Fukai T, Morrison A, Diesmann M (2012) Front Neuroinform 6:26
[5] Kunkel S, Schmidt M, Eppler JM, Plesser HE, Masumoto G, Igarashi J, Ishii S, Fukai T, Morrison A, Diesmann M, Helias M (2014) Front Neuroinform 8:78

Ruben Gur
University of Pennsylvania

The advent of genomic and precision medicine has posed new challenges for neuroimaging and neurocognition. Instead of disjointed studies using single neuroimaging modalities and traditional paper-and-pencil neuropsychological testing, the field has been moving toward multimodal neuroimaging and computerized neurocognitive batteries that evaluate behavioral domains linked to regional brain anatomy and physiology. We describe an effort to ascend to this level of data acquisition and analysis by collecting the Philadelphia Neurodevelopmental Cohort (PNC), in which nearly 10,000 children age 8-21 were studied during 2009-2011 with a comprehensive battery of clinical and neurocognitive assessments and multimodal neuroimaging of 1,600 of these participants. We will describe the study and present initial results from analyzing these data to obtain information

on the relationship between cognitive development and brain maturation. Thje analysis revealed marked sex differences in developmental trajectories.

Raquel Gur
University of Pennsylvania

While the prevalence of schizophrenia in the general population is estimated at about 1% worldwide, there is increased realization that the number of individuals who suffer from psychosis is quite larger and of those who suffer from prominent and disabling psychotic features is larger yet. There is lack of population-based neurodevelopmental studies to help predict transition to psychosis and gauge the neurocognitive and neuroimaging parameters indicative of vulnerability or resilience. We report results from large-scale studies, culminating in the Philadelphia Neurodevelopmental Cohort (PNC), which evaluated neurocognitive and brain imaging parameters in populations at risk for psychosis. Neurocognitive deficits and abnormalities in maturation of brain anatomy, physiology and connectivity can help identify at-risk youths and may suggest avenues for early detection and possibly intervention. The interplay between genetic vulnerability and environmental factors leading to exacerbation or resilience can be documented in such large-scale genomic investigations, especially when follow-up is incorporated.

Greg Farber
NIMH

"The BRAIN Initiative, NIH, and Support for Computational Neuroscience"

NIH has a number of different programs that support extramural research proposals from computational researchers. This presentation will briefly describe programs that have been around for some time. The bulk of the presentation will focus on two large new NIH initiatives: Big Data to Knowledge (BD2K), and the BRAIN Initiative. The BRAIN Initiative is planning a number of new research initiatives that will be open to or will expect the participation of computational researchers.

Polina Golland
MIT

"From Pixels to Brain Networks: Modeling Brain Connectivity and Its Changes in Disease"

We develop a probabilistic framework to model connectivity patterns in the brain as a latent network graph. In particular, we model the interaction between latent anatomical and functional connectivity and present an intuitive extension to population studies. The method simultaneously infers the templates of latent connectivity for each population and the differences in connectivity between the groups. We also develop an approach to identify foci of a neurological disorder based on anatomical and functional connectivity information. Specifically, we formulate a generative model that characterizes the network of abnormal functional connectivity emanating from the affected nodes. We demonstrate our methods on a schizophrenia study. Our model identifies significant increases in functional connectivity between the parietal/posterior cingulate region and the frontal lobe and reduced functional connectivity between the parietal/posterior cingulate region and the temporal lobe in schizophrenia.

Joint work with Archana Venkataraman, Marek Kubicki, Carl-Fredrik Westin.

James Haxby
Darmouth University

"A Common Model of Representational Spaces in Human Cortex".

The functional architecture of human cortex can be modeled as high-dimensional representational spaces in which patterns of brain activity are recast as vectors with basis functions that have tuning profiles and patterns of connectivity that are common across brains. Transformation matrices that rotate individual anatomical spaces into the common model space are derived with searchlight-based, whole cortex hyperalignment. Patterns of brain activity in individual brains are modeled as multiplexed topographic basis functions. This model provides a common structure that captures fine-grained distinctions among cortical patterns of response that are not modeled well by current brain atlases.

Stephanie Jones
Brown University

"Biophysically Principled Computational Modeling of Human MEG/EEG Signals to Link Mechanism to Function"

Magneto- and Electro-encephalography (MEG/EEG) are among the most powerful technologies to non-invasively record large-scale activity from humans with fine temporal and spatial resolution. These signals provide reliable markers of healthy cognitive function and disease processes. However, a major limitation is the difficulty in inferring the underlying cellular and network level activity that generates the recorded data. A cellular level understanding is necessary to design targeted treatments, via pharmacology or brain stimulation (e.g. TMS, tDCS), when these signals are disrupted in neuropathology. In this talk, I will discuss the use of biophysically principled computational neural models of MEG/EEG signals as a viable means to link brain mechanisms to function. I will emphasize the necessity of moving beyond reduced models of neural activity to designing models that account for the electro-magnetic physics of these signals. I will describe our recent development of a laminar model of sensory cortex that accurately reflects the current sources underlying MEG/EEG enabling an interpretive bridge between the macroscopic scale recordings and the underlying cellular and circuit dynamics. This model has led to novel hypothesis on the origin of sensory evoked responses and low frequency rhythms. I will focus on studies of beta frequency rhythms (15-29Hz), which we have observed predict successful tactile detection, are modulated with attention in coordination with frontal cortex, and increase with healthy adult aging. Our model methods and results provide unique insight into the meaning of these rhythms in function. Lastly, I will describe studies designed to test the model-derived predictions with invasive electrophysiological recordings in monkeys and mice.

Rob Kass
Carnegie Mellon University

"A Statistical Perspective on Spike Train Analysis, and Possible Connections with Modeling"

To provide some background for a chunk of this workshop, I will start by saying something about the nature of spike train recordings, and will give my own summary of the traditional questions asked by statisticians and modelers. After defining the point process regression framework (based primarily on generalized linear models — GLMs) I will very briefly define integrate-and-fire neurons and

biophysical, Hodgkin-Huxley neurons. With this, I will mention some points of contact between these two very different approaches, and will list several outstanding issues.

Martin Lindquist
Johns Hopkins University

"Principles of Functional Neuroimaging"

Functional neuroimaging can be used to investigate the living, functioning human brain as people perform tasks and experience mental states. It is a convergence point for multidisciplinary work from many disciplines. Psychologists, statisticians, physicists, computer scientists, neuroscientists, medical researchers, behavioral scientists, engineers, public health researchers, biologists, and others are coming together to advance our understanding of the human mind and brain. In this talk we introduce various functional neuroimaging techniques, including positron emission tomography (PET), functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG). We will particularly focus on data acquisition, experimental design, analysis, and how these techniques can be used to perform inferences about brain and mind.

Wei Ji Ma
New York University

"The Inevitability of Probability: Near-Optimal Probabilistic Inference in Generic Neural Networks Trained with Non-Probabilistic Feedback"

Animals have been shown to perform near-optimal probabilistic inference in a wide range of psychophysical tasks, from causal inference to cue combination to visual search. On the face of it, this is surprising because optimal probabilistic inference in each case is associated with highly non-trivial behavioral strategies. Yet, typically animals receive little to no feedback during most of these tasks and the received feedback is generally not probabilistic in nature. How can animals learn such non-trivial behavioral strategies from scarce non-probabilistic feedback? Here, we show that generic feed-forward and recurrent neural networks trained with very few non-probabilistic examples using simple error-based learning rules can perform near-optimal probabilistic inference. The trained networks implement fully probabilistic strategies as evidenced by the fact that the precision of relevant posteriors can be reliably read out from the pooled activities of subsets of neurons in the network. In many cases, the trained networks also display remarkable generalization to stimulus conditions not seen during training. Our results suggest that far from being difficult to learn, optimal probabilistic inference emerges naturally and robustly in generic neural networks trained with error-based learning rules, even when neither the training objective nor the training examples are probabilistic.

"Growing up in science"

Have you ever wondered what your advisor was like as a graduate student? What they struggled with? What they are struggling with now? This informal discussion for students and postdocs will not be about science, but about becoming and being a scientist. How do you deal with your own and others' expectations, and with impostor syndrome? How do you keep yourself motivated? Wei Ji Ma <http://www.cns.nyu.edu/malab/> (NYU) will tell his personal story and then guide a conversation about the human factors that are universal undercurrents of working in academia but that too often remain unspoken.

Michael Miller
Johns Hopkins University

"Neuroinformatics and the Complexity of the Brain at the 1mm Morphome Scale"

We examine the computational anatomy model, orbits of functional and structural imagery under the action of the diffemorphism group. A geodesic positioning system is described for positioning neuroanatomy within the orbit. The coordinates of the GPS will be examined, deriving methods for clustering and disease prediction on elements of the orbit. Applications to several neurodegenerative diseases, Alzheimer's and Huntington's will be presented. Results on the spatiotemporal flow of neurodegenerative disease associated to cortical and subcortical networks will be shown.

Thomas Nichols
University of Warwick

"Two Wildly Different Approaches to Brain Connectivity in fMRI"

In the last 5 years in neuroimaging there has been a dramatic shift in focus from "brain mapping", identifying brain regions related to particular functions, to connectivity or "connectomics", identifying networks of coordinated brain regions, and how these networks behave at rest and during tasks. In this presentation I will discuss two quite different approaches to modeling brain connectivity. In the first work, we use Bayesian time series methods to allow for time-varying connectivity. Non-stationarity connectivity methods typically use a moving-window approach, while this method poses a single generative model for all nodes, all time points. Known as a "Multiregression Dynamic Model" (MDM), it comprises an extension of a traditional Bayesian Network (or Graphical Model), by posing latent time-varying coefficients that implement a regression a given node on its parent nodes. Intended for a modest number of nodes (up to about 12), a MDM allows inference of the structure of the graph using closed form Bayes factors (conditional on a single estimated "discount factor", reflecting the balance of observation and latent variance. While originally developed for directed acyclic graphs, it can also accommodate directed (possibly cyclic) graphs as well. In the second work, we use mixtures of simple binary random graph models to account for complex structure in brain networks. In this approach, the network is reduced to a binary adjacency matrix. While this is invariably represents a loss of information, it avoids a Gaussianity assumption and allows the use of much larger graphs, e.g. with 100's of nodes. Daudin et al. (2008) proposed a "Erdos-Reyni Mixture Model", which assumes that, after an unknown number of latent node classes have been estimated, that connections arise as Bernoulli counts, homogeneously for each pair of classes. We extend this work to account for multisubject data (where edge data are now Binomially distributed), allowing for covariates and, finally, random intercepts by subject. We illustrate each of these methods with simulated and real data, and show how they address fundamental shortcomings of existing methods.

Friedrich Sommer
University of California, Berkeley

"Understanding the Functions of Oscillatory LFP"

Extracellular multi-electrode recordings allow to isolate spiking activity but also yield the slower and often periodic local field potentials (LFP) that reflect a superposition of spiking, synaptic and subthreshold activity. While impulse-like waveforms (spikes) and periodic waves (oscillatory LFP) coexist in such recordings, most current efforts in data acquisition, analysis and modeling focus on the spiking activity. Although correlations of oscillatory activity with brain function and behavior have

been shown empirically, the computations enabled by brain waves and their interaction with spikes are still unclear. My talk will describe two recent forays in this direction. The first part describes a method how to quantify the amount of information a spike train carries about an oscillatory intrinsic brain signal observed simultaneously.

The second part of the talk describes the recent finding that oscillatory LFPs carry exclusively detailed behavioral information. In the hippocampus of a navigating rat, place neurons discharge selectively when the rat is at certain locations. In contrast, the LFPs during navigation exhibit a powerful traveling wave at 9Hz propagating through the hippocampus and exhibit very little place-tuning at single anatomical sites. It was believed that the 9Hz wave represents the animals behavioral state but by itself contains little specific information about the animals behavior. We could recently demonstrate quite the contrary: the LFP structure at multiple sides contains detailed information about the place of the animal. Specifically, the location of the animal can be decoded from the LFP with comparable precision as from the spike trains detected in the same recordings.